ISSN: 0974-5343
IJMST (2010), 3(2):9-16

Use of statistical methods in predicting Acute Hypotensive Episodes

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ABSTRACT:
The variation with time of arterial blood pressure (ABP) and the variation of the beating of the heart form well defined Time Series. Irregularities in the pumping mechanism of the heart lead to acute hypotension, or low blood pressure. Frequent episodes of acute hypotension aggravate the other medical problems of gravely critical patients, therefore acute hypotensive episodes (AHE) are monitored in the intensive care units (ICU) as forecasters of the sinking condition of a critically ill patient. Prediction of an AHE is important in the care of patients in the ICU. This paper presents an automatic predictor for AHE using simple statistical methods which have a reasonably high specificity.

Key words: Time Series, PhysioNet.

INTRODUCTION

The heart is a muscle that pumps blood around the body continuously. The pumping of blood generates pressure – Arterial Blood Pressure (ABP). Our ABP is measured by both the systolic (when heart contracts) and diastolic (when heart rests) pressures. If the systolic pressure is between 90 to 119 mmHg and diastolic pressure is between 60 to 79 mmHg then ABP is said to be normal. Anybody with a reading of below 90 in systolic and below 60 mmHg in diastolic blood pressure is regarded as having hypotension (low ABP) [1, 2].

One of the several grave conditions that may seriously damage the already critical condition of a patient in the intensive care unit (ICU) is an episode of acute hypotension. These acute hypotension episodes (AHE) require prompt and effective intervention to prevent irreversible damage to the organs and probable death. Incidents of AHE may be caused by insufficient cardiac output, vaso-dilatory shock, myocardial infarction and cardiac arrhythmia among abnormal cardiac conditions. But sometimes an episode may be caused simply by dehydration or sepsis.

A strategy in intensive care of critical patients is to find a suboptimal, but relatively safe method of intervention until a more effective treatment can be found suitable for the patient. This is where prediction of AHE is important. By observing the Time Series of ABP of patients and comparing it to that of the control group, as provided by PhysioNet [3], we could predict the episodes of AHE with reasonably high specificity.

Time series analysis of ABP has given good results in terms of periodicity and harmonics. The ABP signal is periodic signal which can be studied well by using Fourier techniques. Most of the energy of ABP signal is contained in these harmonics [4, 5].

PROBLEM AND MATERIALS

PhysioNet is a web based resource supplying well characterized physiological signals and related open source software to the Biomedical research community. In cooperation with the annual Computers in Cardiology conference, PhysioNet hosts a series of **"challenges"**, inviting participants to tackle clinically interesting problems that are either unsolved or not well-solved.

The challenge dataset includes, for each case, a time series of Mean Arterial Blood Pressure (MBP) at one-minute intervals. Each sample of the series is an average of the blood pressure measured in the radial artery over the previous minute. In the PhysioNet/Computers in Cardiology Challenge 2009, researchers were asked to predict which patients in the challenge dataset will experience an AHE beginning within the forecast window [6].

An AHE is defined for the purposes of this challenge as any period of 30 minutes or more during which at least 90% of the MBP measurements were at or below 60 mmHg.

The training and test data sets are provided as illustrated in Figure 1. Challenge participants were asked to develop automated techniques for predicting AHE up to an hour in advance in selected ICU patient records, using any data available before the forecast window for each record.

For each case, we chose a specified time, T_0, at least 10 hours after the beginning of the MBP time series. Participants used the portion of each record occurring before T_0 to predict if an AHE would begin during the hour following T_0, the forecast window. Further details of the Challenge are provided in [7].

H1 (AHE treated with pressors*) (n=15)	H2 (AHE not treated with pressors) (n=15)
C1 (no AHE) (n=15)	C2 (AHE outside the forecast window) (n=15)

(a)

H1 (AHE, receiving pressors) (n=5)	C1 (no AHE, receiving pressors) (n=5)

(b)

H (AHE in forecast window) (16≥n≥10)	C (no AHE in forecast window) (30≥n≥24)

(c)

Figure 1: Schematic diagram of (a) Training Set, (b) Test Set A, and (c) Test Set B; where n is number of patients.
***A pressor is a substance capable of raising the blood pressure .**

To enter case 1, we have to design and implement an automated method to identify which of the records in test set A belong to subgroup H1 (AHE treated with pressors) and to enter case 2, we have to design and implement an automated method to identify which of the records in test set B belong to group H (AHE in forecast window). In case 1, H1 (AHE, in subjects receiving pressors) and modified C1 (no AHE, in subjects receiving pressors) subgroups of test set A represent extremes of AHE-associated risk. Case 2 aims to address the broad question of predicting AHE in a population in which about a third of the patients experience AHE.An algorithm was designed to find an alternate method of predicting an AHE, by using training sets of subgroup H1 (AHE treated with pressors), subgroup H2 (AHE not treated with pressors), subgroup C1 (no AHE) and subgroup C2 (AHE outside the forecast window) and to test it against test set A and test set B for case 1 and case 2 respectively.

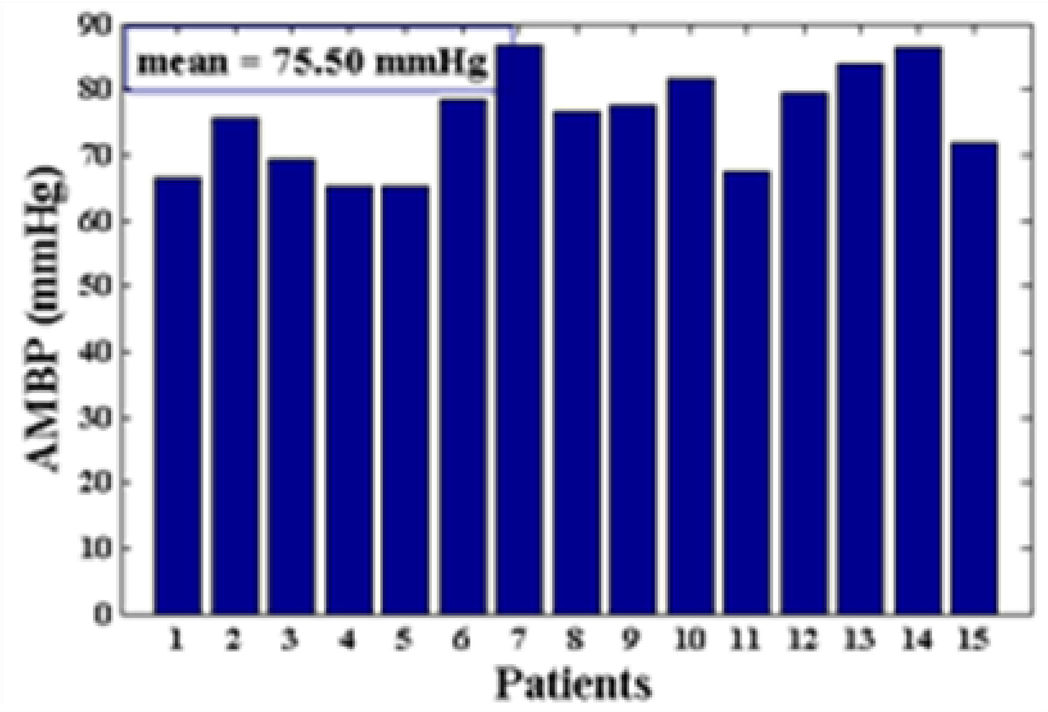
METHODOLOGY

A Time Series is an ordered sequence of data points made at specified time (or space) intervals. The systematic approach by which one goes about answering the mathematical and statistical questions posed by time (or space) correlations is commonly referred to as time series analysis. Time series analysis is concerned with quantifying the order and correlations, if any, of data points. Spectral analysis of the MBP and ABP time series is done by applying the Fast Fourier Transform (FFT) method [8, 9].

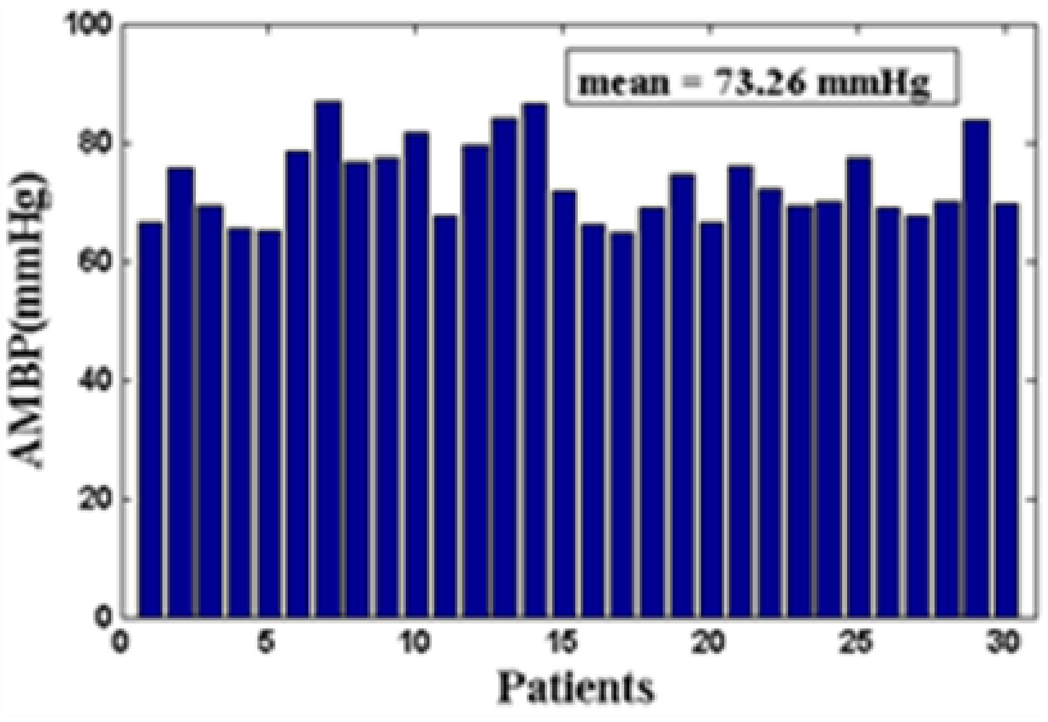
The nature of subjects of test set A and test set B is relatively different. The subjects of test set A are either highly prone to AHE or absolutely not. While in test set B, subjects are in the decreasing order of risk ($H_1 > H_1 > C_2 > C_1$) hence it is a complex set of data. Thus at the time of deciding strategy for prediction we have to be more selective in conditions for test set B than for test set A. In predicting AHE, we have used Average of MBP (AMBP) as a primary marker. In Figure 2 bar graphs of training sets for AMBP are given. The average value of AMBPs is 75.50 mmHg for subgroup H1 and 73.26 mmHg for combined subgroups H1 and H2. We performed t-test on AMBP time series to analyze data whether it is significant or not. After taking mean of ABP, it is necessary to be sure that data is carrying meaningful information for AHE prediction. We have taken two unpaired groups, healthy and unhealthy for performing unpaired t-test for each set separately [10]. An algorithm has been developed to predict AHE in case 1 and case 2. Flowchart is shown in Fig. 3. For each scanning and analysis of data, there are two parameters in algorithm (1) R- the number of data below 60 mmHg, and (2) K- the number of times R is true. The values of parameters of algorithms used for case 1 and case 2 are different on the basis of results coming from training sets.

RESULTS

For case 1, the training set H_1 is being analyzed and AMBP as a marker is on 75.50 mmHg. So the subjects whose AMBP is blow 75.50 mmHg are said to be hypotensive. In test set A, AMBP of four patients are greater than 75.50 mmHg. After getting clue from H_1 and C_1 training subgroups, we have applied algorithm with parameters $R > 0$ and $K > 0$ on test set A, with the result given as 7 AHE prone subjects. But according to challenge [3], there are 5 patients of AHE in test set A. So we have changed the values of threshold AMBP and parameters R and K. The new values are 72 mmHg [Fig. 4(a)] of AMBP and $R > 1$ and $K > 0$, and using these values 100% correct results are obtained. For case 2, we have taken the subgroups H1 and H2 of training set into our account. AMBP threshold is set to be 73.26 mmHg [Fig. 4(a)] and when applied on test set B, giving 70.59% correct results, according to concluded result of challenge. The values of R and K from training set subgroup H_1 and C_1 and subgroup H_2 and C_2 are ($R > 0$, $K > 0$) and ($R > 4$, $K > 0$) respectively. We have applied our algorithm with the values $R > 4$, $K > 0$ on test set B with 73.53% success. But when values $R > 6$, $K > 0$ is being used in the algorithm 79.41% results were correct. For unpaired t-test, the two-tailed P value equals 0.0097 and 0.0214 for test set A and test set B, respectively[Table1].



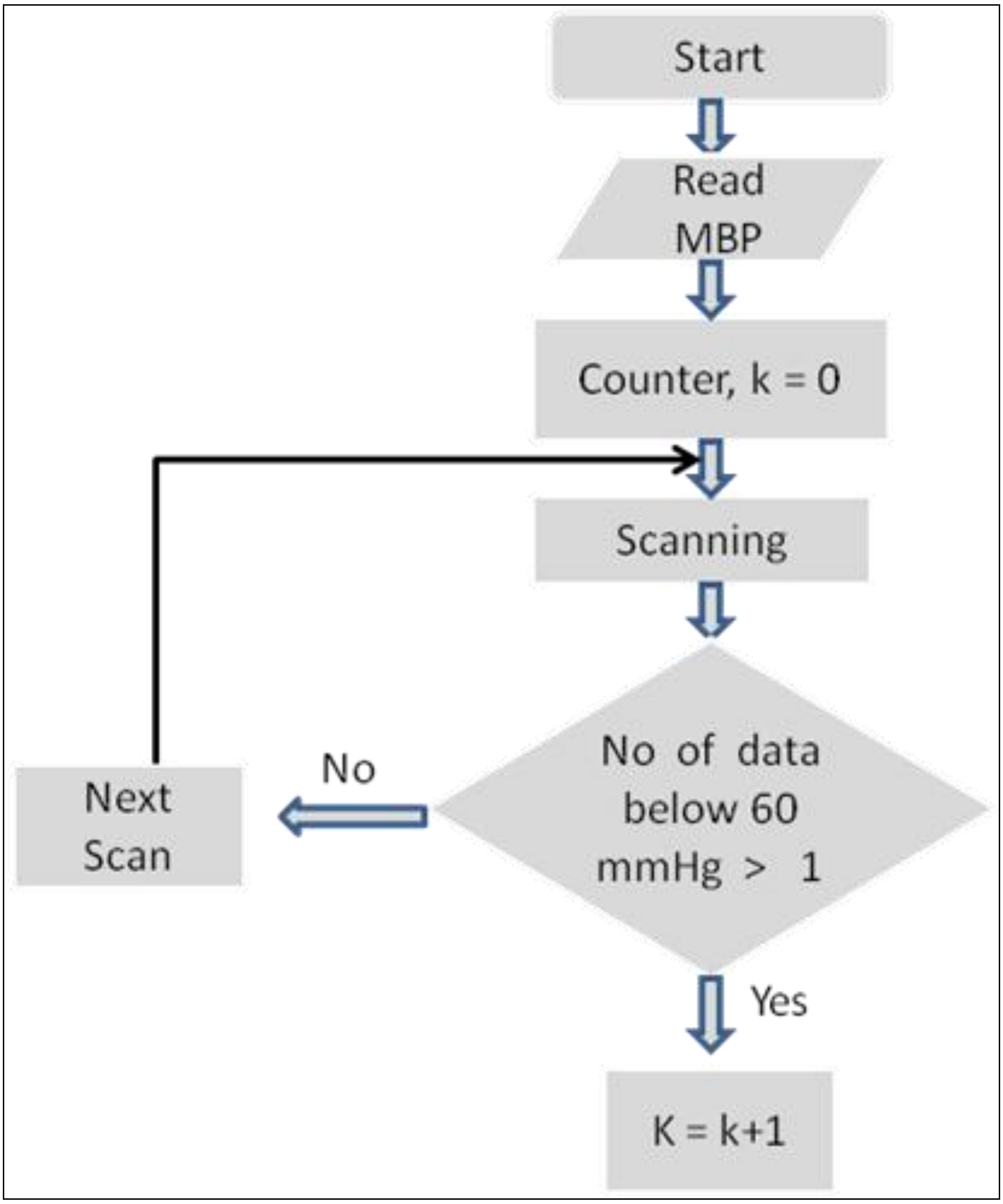
(a)



(b)

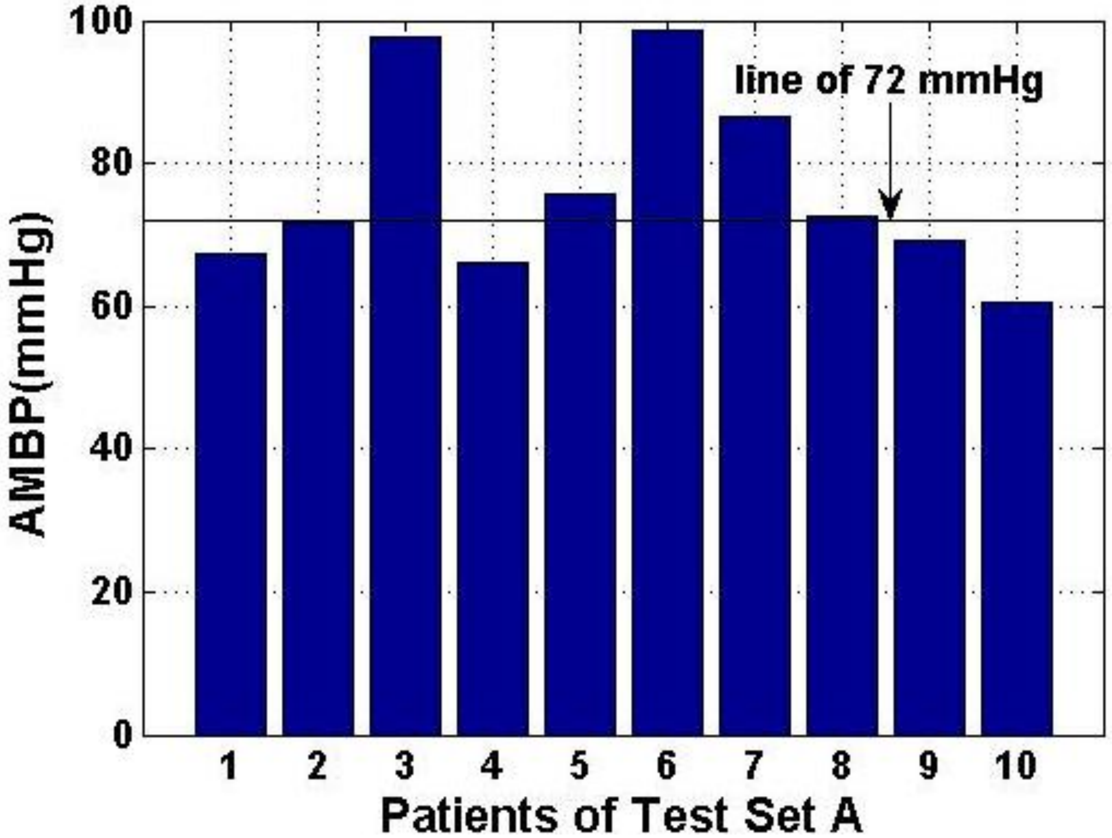
Figure 2: Bar diagram of (a) Training Set H_1, and (b) Training set H_1 and H_2

ISSN: 0974-5343
IJMST (2010), 3(2):9-16

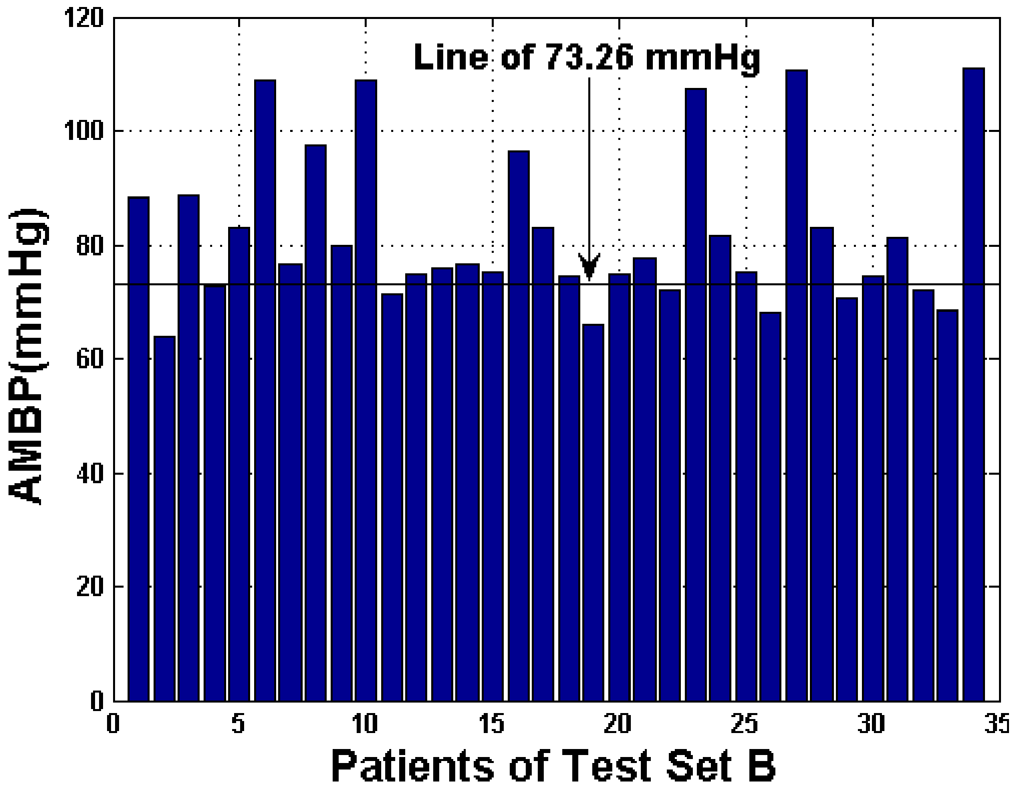


Flow Chart

Figure 3: Flowchart for scanning Mean Arterial Blood Pressure (MBP) series for counting the data which is below 60 mmHg.

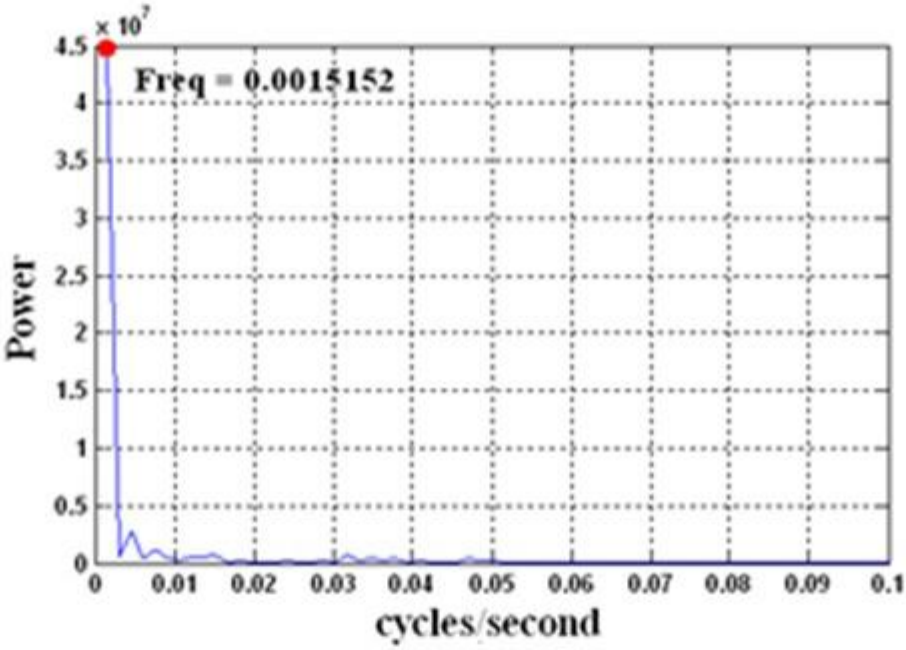


(a)

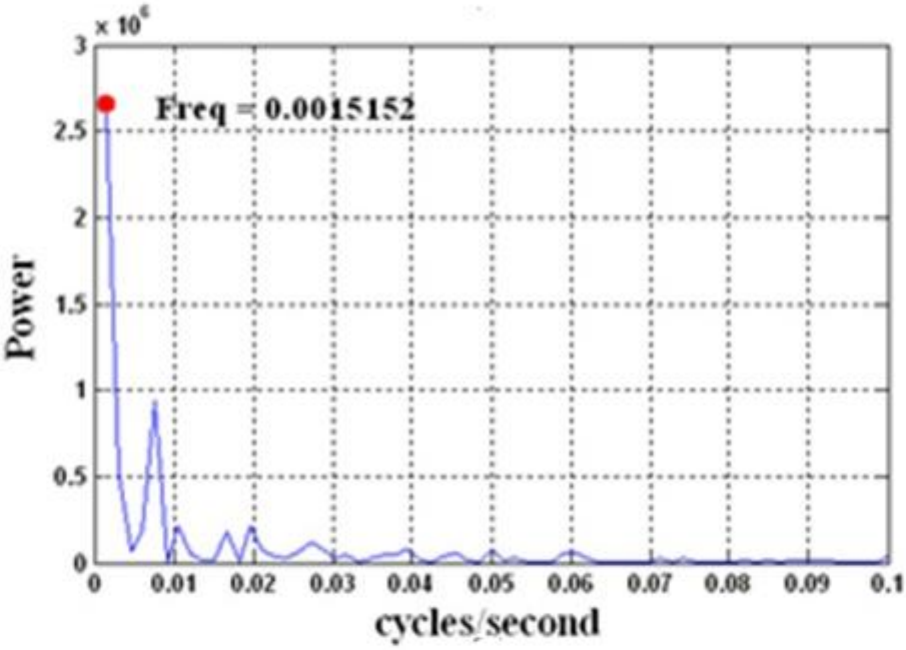


(b)

Figure 4: Bar diagram of Average of Mean Arterial Blood Pressure (AMBP) of (a) Test Set A, and (b) Test Set B


x 10^7
Freq = 0.0015152
Power
cycles/second
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.1

(a)


x 10^6
Freq = 0.0015152
Power
cycles/second
3
2.5
2
1.5
1
0.5
0
0
0.01
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0.03
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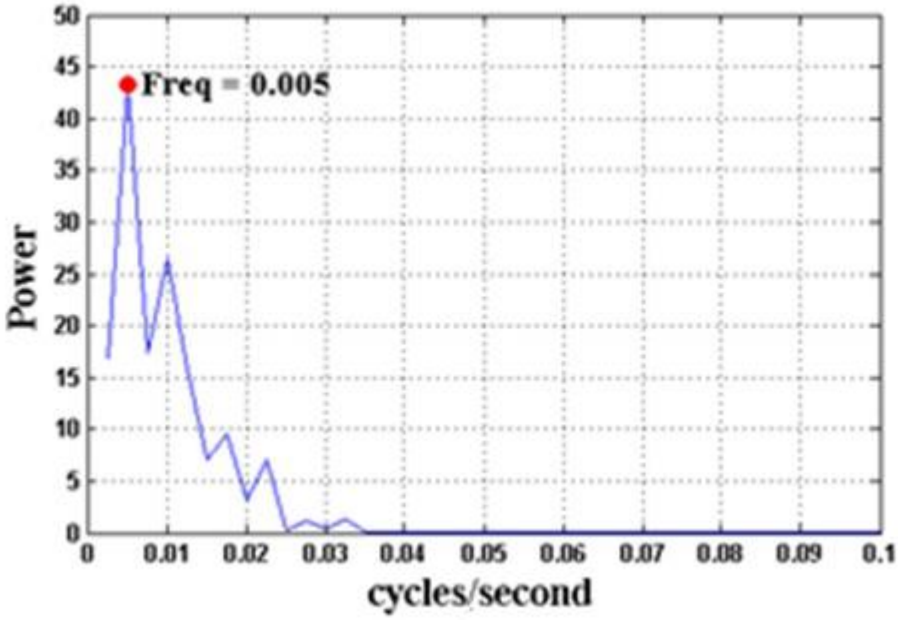
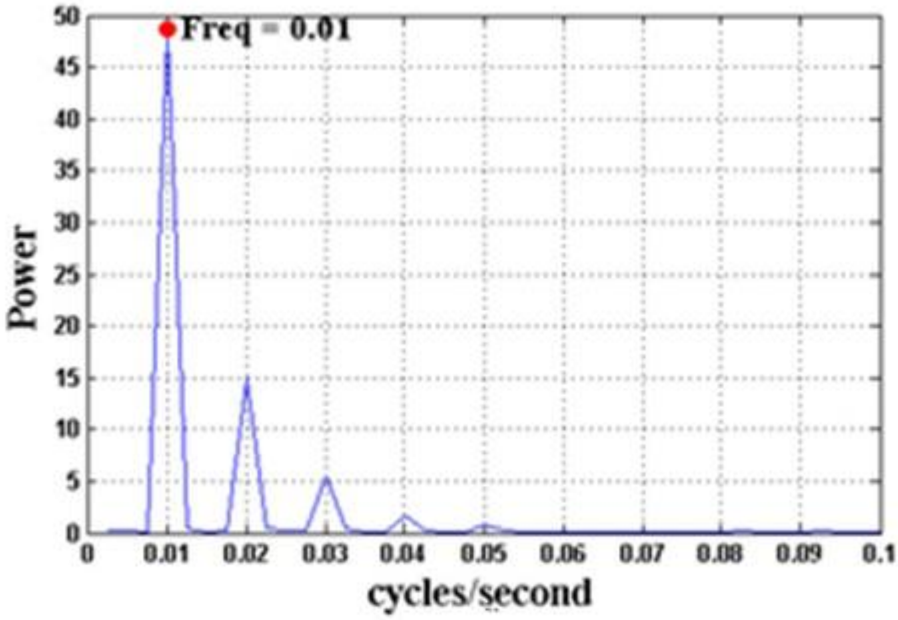
0.05
0.06
0.07
0.08
0.09
0.1

(b)



(c)



(d)

Figure 5: Power spectra of MBP time series of (a) of subgroup H_1 (b) of subgroup C_1, of training set; Power spectra of ABP time series of record number (c) of test set A which is of H_1 subgroup, and (d) of C_1 subgroup.

IJMST

ISSN: 0974-5343
IJMST (2010), 3(2):9-16

By conventional criteria this result is very significant for test set A and significant for test set B. The t-test is proving the significance of data of MBP, which is ensuring us that after taking mean of ABP time series for each 7500 data(because each ABP datum is at 0.008 second interval), the new set of data (i.e. MBP) is still significant and can be used to predict AHE in forecast window one hour in advance.

Table 1: p- value for unpaired t-test for test set A and test set B

	Test Set A	Test Set B
p- value	0.0097	0.0214

Table 1 shows the p-value for unpaired t-test for test set A and test set B for two unpaired group, healthy and unhealthy for each test set

When Fast Fourier Transform (FFT) is applied on the MBP time series, the results are ambiguous as seen in Figure 5(a) and 5(b) where 5(a) corresponds to numeric record number a41882n of subgroup H1 and 5(b) corresponds to numeric record number a41466n of subgroup C1 of training set.

But power spectra of ABP time series data can be effectively used for the prediction of AHE in the forecast window. For hypotensive subjects power spectra show irregularities, or non-harmonic nature, whereas non-hypotensive subjects graphs of power spectra are regular and harmonics are well expressed [Fig. 5(c) and 5(d) respectively].

DISCUSSION AND CONCLUSIONS

The mortality rate of hypotensive patients is very high in ICUs and episodes of AHE require effective, prompt intervention. Left untreated, such episodes may result in irreversible organ damage and death. By taking proper care of possibilities of AHE in advance, mortality rate can be decreased. Training sets of different conditions are provided and by using training sets we have developed an algorithm for both test set A and test set B.

We have shown that AMBP can efficiently predict the AHE in forecast window. Occurrence of lower values of AMBP indicates greater probability of AHE. The t-test result is very significant for test set A because this test set represent extremes of AHE-associated risk. Whereas t-test result is merely significant for test set B, which can be explained in terms of presence of whole range of AHE-associated risk.

Therefore the results of the algorithm are also as efficient as AMBP in predicting the AHE in forecast window. The different values of AMBP and other parameters of the algorithm used are due to difference of domain of the subjects.

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Abbreviations: AHE, ABP, MBP, AMBP.